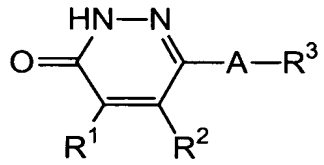
CLAIMS

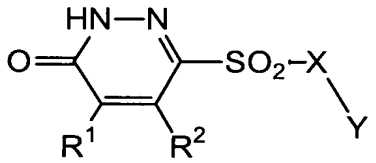
1. A pharmaceutical composition comprising a first compound selected from:

a compound of formula I



I,

and a compound of formula II



II,

or a prodrug of said first compound, or a pharmaceutically acceptable salt of said first compound or said prodrug,

wherein:

A is S, SO or SO_2;

R^1 and R^2 are each independently hydrogen or methyl;

R^3 is Het^1, $-CHR^4Het^1$ or NR^6R^7;

R^4 is hydrogen or $(C_1\text{-}C_3)$alkyl;

R^6 is $(C_1\text{-}C_6)$alkyl, aryl or Het^2;

R^7 is Het^3;

Het^1 is pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl, pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl,

imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl, imidazolopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; Het^1 is independently optionally substituted with up to a total of four substituents independently selected from R^8, R^9, R^{10} and R^{11}; wherein R^8, R^9, R^{10} and R^{11} are each taken separately and are each independently halo, formyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylenyloxycarbonyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C(OH)R^{12}R^{13}$, $(C_1$-$C_4)$alkylcarbonylamido, $(C_3$-$C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1$-$C_4)$alkylsulfenyl, $(C_1$-$C_4)$alkylsulfonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to three fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to two substituents independently selected from hydroxy, halo, C_1-$C_4)$alkyl, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, C_1-$C_4)$alkyl-phenyl optionally substituted in the phenyl portion with one Cl, Br, OMe, Me or SO_2-phenyl wherein said SO_2-phenyl is optionally substituted in the phenyl portion with one Cl, Br, OMe, Me, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro, or $(C_1$-$C_4)$alkoxy optionally substituted with up to three fluoro;

R^{12} and R^{13} are each independently hydrogen or $(C_1$-$C_4)$alkyl;

Het^2 and Het^3 are each independently imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy; Het^2 and Het^3 are each independently optionally substituted with up to a total of four substituents independently selected from R^{14}, R^{15}, R^{16} and R^{17}, wherein R^{14}, R^{15}, R^{16} and R^{17} are each taken separately and are each independently halo, formyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylenyloxycarbonyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C(OH)R^{18}R^{19}$, $(C_1$-$C_4)$alkylcarbonylamido, $(C_3$-$C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1$-$C_4)$alkylsulfenyl, $(C_1$-$C_4)$alkylsulfonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to three fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to three fluoro; and

R^{18} and R^{19} are each independently hydrogen or $(C_1$-$C_4)$alkyl;

X and Y together are CH_2-CH(OH)-Ar or CH_2-C(O)-Ar, or

X is a covalent bond, NR^{20} or CHR^{21}, wherein, R^{20} is $(C_1$-$C_3)$alkyl or a phenyl that is optionally substituted with one or more substituents selected

from OH, F, Cl, Br, I, CN, CF_3, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and SO_2—$NR^{22}R^{23}$, and R^{21} is hydrogen or methyl, and

Y is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from Ar, OH, F, Cl, Br, I, CN, CF_3, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and SO_2—$NR^{22}R^{23}$;

Ar is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from F, Cl, Br, I, CN, CF_3, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and SO_2—$NR^{22}R^{23}$;

n is independently for each occurrence 0, 1 or 2;

R^{22} is independently for each occurrence H, $(C_1$-$C_6)$alkyl, phenyl or naphthyl; and

R^{23} is independently for each occurrence $(C_1$-$C_6)$alkyl, phenyl or naphthyl,

provided that when R^3 is NR^6R^7, then A is SO_2; and

a second compound that is a cyclooxygenase-2 inhibitor, a prodrug of said second compound or a pharmaceutically acceptable salt of said second compound or said prodrug.

2. A composition of claim 1 wherein said first compound is a compound of formula I, wherein A is SO_2; R^1 and R^2 are each hydrogen; R^3 is Het^1, wherein Het^1 is 5H-furo-[3,2c]pyridin-4-one-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl, indol-2-yl, indol-3-yl, benzofuran-2-yl, benzothien-2-yl, imidazo[1,2a]pyridin-3-yl, pyrrol-1-yl, imidazol-1-yl, indazol-1-yl, tetrahydroquinol-1-yl or tetrahydroindol-1-yl, wherein said Het^1 is optionally independently substituted with up to a total of two substituents each independently selected from fluoro, chloro, bromo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, trifluoromethyl, hydroxy, benzyl or phenyl; said benzyl and phenyl are each optionally independently substituted with up to three halo, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylsulfinyl, $(C_1$-$C_6)$alkylsulfenyl, trifluoromethyl or hydroxy, or a prodrug thereof or a pharmaceutically acceptable salt of said compound or prodrug.

3 A composition of claim 2 wherein Het^1 is indol-2-yl, benzofuran-2-yl, benzothiophen-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl or imidazo[1,2a]pyridin-4-yl, wherein said Het^1 is optionally independently substituted with up to a total of two substituents independently selected from

fluoro, chloro, bromo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, trifluoromethyl and phenyl; said phenyl being optionally substituted with up to two substituents independently selected from fluoro, chloro and (C_1-C_6)alkyl.

4. A composition of claim 1 wherein said first compound is selected from: 6-(3-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-bromo-2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-bromo-benzenesulfonyl)-2H-pyridazin-3-one;
6-(3,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-methoxy-benzenesulfonyl)-2H-pyridazin-3-one;
6-(3-bromo-benzenesulfonyl)-2H-pyridazin-3-one;
6-(biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(4'-fluoro-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(4'-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(3',5'-bis-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(biphenyl-2-sulfonyl)-2H-pyridazin-3-one;
6-(4'-trifluoromethyl-biphenyl-2-sulfonyl)-2H-pyridazin-3-one;
6-(2-hydroxy-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-chloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(3-chloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,3-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,5-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-chloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,3-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,4-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,6-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-chloro-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-bromo-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one; and
6-(naphthalene-1-sulfonyl)-2H-pyridazin-3-one,

or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

5. A composition of claim 1 wherein said second compound is selected from celecoxib, rofecoxib and etoricoxib or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

6. A pharmaceutical composition of claim 1 wherein said first compound is in an aldose reductase inhibiting amount.

7. A pharmaceutical composition of claim 1 wherein said second compound is present in a cyclooxygenase-2 inhibiting amount.

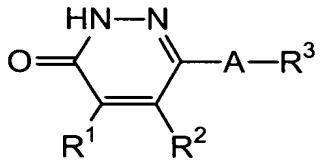
8. A pharmaceutical composition of claim 6 wherein said second compound is present in a cyclooxygenase-2 inhibiting amount.

9. A pharmaceutical composition of claim 1 further comprising a vehicle, diluent or carrier.

10. A kit comprising:

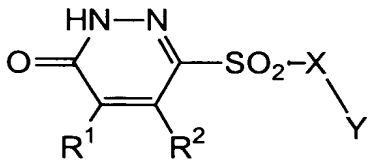
a first dosage form comprising a first compound selected from:

a compound of formula I



I,

and a compound of formula II



II,

or a prodrug of said first compound, or a pharmaceutically acceptable salt of said first compound or said prodrug,

wherein:

A is S, SO or SO_2;

R^1 and R^2 are each independently hydrogen or methyl;

R^3 is Het^1, $-CHR^4Het^1$ or NR^6R^7;

R^4 is hydrogen or $(C_1\text{-}C_3)$alkyl;

R^6 is $(C_1\text{-}C_6)$alkyl, aryl or Het^2;

R^7 is Het^3;

Het^1 is pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl, pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl, imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl, imidazolopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; Het^1 is independently optionally substituted with up to a total of four substituents independently selected from R^8, R^9, R^{10} and R^{11}; wherein R^8, R^9, R^{10} and R^{11} are each taken separately and are each independently halo, formyl, $(C_1\text{-}C_6)$alkoxycarbonyl, $(C_1\text{-}C_6)$alkylenyloxycarbonyl, $(C_1\text{-}C_4)$alkoxy-$(C_1\text{-}C_4)$alkyl, $C(OH)R^{12}R^{13}$, $(C_1\text{-}C_4)$alkylcarbonylamido, $(C_3\text{-}C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1\text{-}C_4)$alkylsulfenyl, $(C_1\text{-}C_4)$alkylsulfonyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_1\text{-}C_4)$alkyl optionally substituted with up to three fluoro or $(C_1\text{-}C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to three substituents independently selected from hydroxy,

halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to two substituents independently selected from hydroxy, halo, C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, C_1-C_4)alkyl-phenyl optionally substituted in the phenyl portion with one Cl, Br, OMe, Me or SO_2-phenyl wherein said SO_2-phenyl is optionally substituted in the phenyl portion with one Cl, Br, OMe, Me, (C_1-C_4)alkyl optionally substituted with up to five fluoro, or (C_1-C_4)alkoxy optionally substituted with up to three fluoro;

R^{12} and R^{13} are each independently hydrogen or (C_1-C_4)alkyl;

Het^2 and Het^3 are each independently imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy; Het^2 and Het^3 are each independently optionally substituted with up to a total of four substituents independently selected from R^{14}, R^{15}, R^{16} and R^{17}, wherein R^{14}, R^{15}, R^{16} and R^{17} are each taken separately and are each independently halo, formyl, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylenyloxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, $C(OH)R^{18}R^{19}$, (C_1-C_4)alkylcarbonylamido, (C_3-C_7)cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, (C_1-C_4)alkylsulfenyl, (C_1-C_4)alkylsulfonyl, (C_3-C_7)cycloalkyl, (C_1-C_4)alkyl optionally substituted with up to three fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally

substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to three fluoro; and

R^{18} and R^{19} are each independently hydrogen or (C_1-C_4)alkyl;

X and Y together are CH_2-CH(OH)-Ar or CH_2-C(O)-Ar, or

X is a covalent bond, NR^{20} or CHR^{21}, wherein, R^{20} is (C_1-C_3)alkyl or a phenyl that is optionally substituted with one or more substituents selected from OH, F, Cl, Br, I, CN, CF_3, (C_1-C_6)alkyl, O-(C_1-C_6)alkyl, $S(O)_n$-(C_1-C_6)alkyl and SO_2—$NR^{22}R^{23}$, and R^{21} is hydrogen or methyl, and

Y is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from Ar, OH, F, Cl, Br, I, CN, CF_3, (C_1-C_6)alkyl, O-(C_1-C_6)alkyl, $S(O)_n$-(C_1-C_6)alkyl and SO_2—$NR^{22}R^{23}$;

Ar is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from F, Cl, Br, I, CN, CF_3, (C_1-C_6)alkyl, O-(C_1-C_6)alkyl, $S(O)_n$-(C_1-C_6)alkyl and SO_2—$NR^{22}R^{23}$;

n is independently for each occurrence 0, 1 or 2;

R^{22} is independently for each occurrence H, (C_1-C_6)alkyl, phenyl or naphthyl; and

R^{23} is independently for each occurrence (C_1-C_6)alkyl, phenyl or naphthyl,

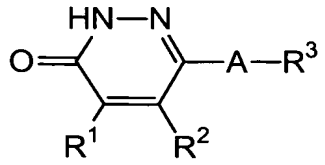
provided that when R^3 is NR^6R^7, then A is SO_2;

a second dosage form comprising a second compound that is a cyclooxygenase-2 inhibitor, a prodrug of said second compound or a pharmaceutically acceptable salt of said second compound or said prodrug; and

a container.

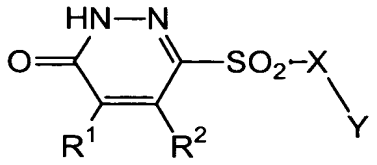
11. A therapeutic method comprising administering to a mammal in need of treatment or prevention of diabetic complications a first compound selected from:

a compound of formula I



I

and a compound of formula II



II,

or a prodrug of said first compound, or a pharmaceutically acceptable salt of said first compound or said prodrug,

wherein:

A is S, SO or SO_2;

R^1 and R^2 are each independently hydrogen or methyl;

R^3 is Het^1, $-CHR^4Het^1$ or NR^6R^7;

R^4 is hydrogen or (C_1-C_3)alkyl;

R^6 is (C_1-C_6)alkyl, aryl or Het^2;

R^7 is Het^3;

Het^1 is pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl, pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl, imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl, imidazolopyridazinyl, oxazolopyridazinyl,

thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; Het^1 is independently optionally substituted with up to a total of four substituents independently selected from R^8, R^9, R^{10} and R^{11}; wherein R^8, R^9, R^{10} and R^{11} are each taken separately and are each independently halo, formyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylenyloxycarbonyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C(OH)R^{12}R^{13}$, $(C_1$-$C_4)$alkylcarbonylamido, $(C_3$-$C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1$-$C_4)$alkylsulfenyl, $(C_1$-$C_4)$alkylsulfonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to three fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to two substituents independently selected from hydroxy, halo, C_1-$C_4)$alkyl, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, C_1-$C_4)$alkyl-phenyl optionally substituted in the phenyl portion with one Cl, Br, OMe, Me or SO_2-phenyl wherein said SO_2-phenyl is optionally substituted in the phenyl portion with one Cl, Br, OMe, Me, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro, or $(C_1$-$C_4)$alkoxy optionally substituted with up to three fluoro;

R^{12} and R^{13} are each independently hydrogen or $(C_1$-$C_4)$alkyl;

Het^2 and Het^3 are each independently imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy,

thiophenoxy; Het^2 and Het^3 are each independently optionally substituted with up to a total of four substituents independently selected from R^{14}, R^{15}, R^{16} and R^{17}, wherein R^{14}, R^{15}, R^{16} and R^{17} are each taken separately and are each independently halo, formyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylenyloxycarbonyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C(OH)R^{18}R^{19}$, $(C_1$-$C_4)$alkylcarbonylamido, $(C_3$-$C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1$-$C_4)$alkylsulfenyl, $(C_1$-$C_4)$alkylsulfonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to three fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to two substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to three fluoro; and R^{18} and R^{19} are each independently hydrogen or $(C_1$-$C_4)$alkyl;

X and Y together are CH_2-CH(OH)-Ar or CH_2-C(O)-Ar, or

X is a covalent bond, NR^{20} or CHR^{21}, wherein, R^{20} is $(C_1$-$C_3)$alkyl or a phenyl that is optionally substituted with one or more substituents selected from OH, F, Cl, Br, I, CN, CF_3, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and SO_2—$NR^{22}R^{23}$, and R^{21} is hydrogen or methyl, and

Y is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from Ar, OH, F, Cl, Br, I, CN, CF_3, $(C_1$-$C_6)$alkyl, O-$(C_1$-$C_6)$alkyl, $S(O)_n$-$(C_1$-$C_6)$alkyl and SO_2—$NR^{22}R^{23}$;

Ar is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from F, Cl, Br, I, CN, CF_3, $(C_1\text{-}C_6)$alkyl, O-$(C_1\text{-}C_6)$alkyl, $S(O)_n$-$(C_1\text{-}C_6)$alkyl and SO_2—$NR^{22}R^{23}$;

n is independently for each occurrence 0, 1 or 2;

R^{22} is independently for each occurrence H, $(C_1\text{-}C_6)$alkyl, phenyl or naphthyl; and

R^{23} is independently for each occurrence $(C_1\text{-}C_6)$alkyl, phenyl or naphthyl,

provided that when R^3 is NR^6R^7, then A is SO_2,

and a second compound that is a cyclooxygenase-2 inhibitor, a prodrug of said second compound or a pharmaceutically acceptable salt of said second compound or said prodrug.

12. A therapeutic method of claim 11 wherein said first compound is a compound of formula I, wherein A is SO_2; R^1 and R^2 are each hydrogen; R^3 is Het^1, wherein Het^1 is 5H-furo-[3,2c]pyridin-4-one-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl, indol-2-yl, indol-3-yl, benzofuran-2-yl, benzothien-2-yl, imidazo[1,2a]pyridin-3-yl, pyrrol-1-yl, imidazol-1-yl, indazol-1-yl, tetrahydroquinol-1-yl or tetrahydroindol-1-yl, wherein said Het^1 is optionally independently substituted with up to a total of two substituents each independently selected from fluoro, chloro, bromo, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, trifluoromethyl, hydroxy, benzyl or phenyl; said benzyl and phenyl are each optionally independently substituted with up to three halo, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylsulfonyl, $(C_1\text{-}C_6)$alkylsulfinyl, $(C_1\text{-}C_6)$alkylsulfenyl, trifluoromethyl or hydroxy, or a prodrug thereof or a pharmaceutically acceptable salt of said compound or prodrug.

13. A therapeutic method of claim 12 wherein Het^1 is indol-2-yl, benzofuran-2-yl, benzothiophen-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl or imidazo[1,2a]pyridin-4-yl, wherein said Het^1 is optionally independently substituted with up to a total of two substituents independently selected from fluoro, chloro, bromo, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, trifluoromethyl and phenyl; said phenyl being optionally substituted with up to two substituents independently selected from fluoro, chloro and $(C_1\text{-}C_6)$alkyl.

14. A therapeutic method of claim 11 wherein said first compound is selected from: 6-(3-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-bromo-2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-bromo-benzenesulfonyl)-2H-pyridazin-3-one;
6-(3,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-methoxy-benzenesulfonyl)-2H-pyridazin-3-one;
6-(3-bromo-benzenesulfonyl)-2H-pyridazin-3-one;
6-(biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(4'-fluoro-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(4'-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(3',5'-bis-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;
6-(biphenyl-2-sulfonyl)-2H-pyridazin-3-one;
6-(4'-trifluoromethyl-biphenyl-2-sulfonyl)-2H-pyridazin-3-one;
6-(2-hydroxy-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-chloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(3-chloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,3-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,5-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(4-chloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,3-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,4-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2,6-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-chloro-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;
6-(2-bromo-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one; and
6-(naphthalene-1-sulfonyl)-2H-pyridazin-3-one,

or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

15. A therapeutic method of claim 11 wherein said second compound is selected from celecoxib, rofecoxib and etoricoxib or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

16. A therapeutic method of claim 11 wherein said first compound is administered in an aldose reductase inhibiting amount.

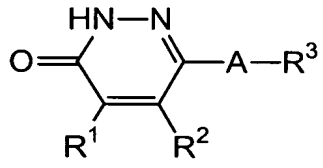
17. A therapeutic method of claim 11 wherein said second compound is administered in a cyclooxygenase-2 inhibiting amount.

18. A therapeutic method of claim 16 wherein said second compound is administered in a cyclooxygenase-2 inhibiting amount.

19. A therapeutic method of claim 11 wherein said mammal is a human.

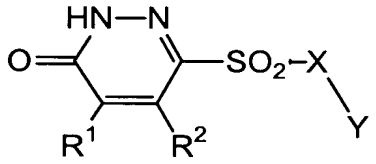
20. A therapeutic method comprising administering to a mammal in need of treatment or prevention of cardiac tissue ischemia a first compound selected from:

a compound of formula I



I,

and a compound of formula II



II,

or a prodrug of said first compound, or a pharmaceutically acceptable salt of said first compound or said prodrug,

wherein:

A is S, SO or SO_2;

R^1 and R^2 are each independently hydrogen or methyl;

R^3 is Het^1, $-CHR^4Het^1$ or NR^6R^7;

R^4 is hydrogen or $(C_1\text{-}C_3)$alkyl;

R^6 is $(C_1\text{-}C_6)$alkyl, aryl or Het^2;

R^7 is Het^3;

Het^1 is pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, quinazolyl, quinoxalyl, phthalazinyl, cinnolinyl, naphthyridinyl, pteridinyl, pyrazinopyrazinyl, pyrazinopyridazinyl, pyrimidopyridazinyl, pyrimidopyrimidyl,

pyridopyrimidyl, pyridopyrazinyl, pyridopyridazinyl, pyrrolyl, furanyl, thienyl, imidazolyl, oxazolyl, thiazolyl, pyrazolyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzothiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, pyrrolopyridyl, furopyridyl, thienopyridyl, imidazolopyridyl, oxazolopyridyl, thiazolopyridyl, pyrazolopyridyl, isoxazolopyridyl, isothiazolopyridyl, pyrrolopyrimidyl, furopyrimidyl, thienopyrimidyl, imidazolopyrimidyl, oxazolopyrimidyl, thiazolopyrimidyl, pyrazolopyrimidyl, isoxazolopyrimidyl, isothiazolopyrimidyl, pyrrolopyrazinyl, furopyrazinyl, thienopyrazinyl, imidazolopyrazinyl, oxazolopyrazinyl, thiazolopyrazinyl, pyrazolopyrazinyl, isoxazolopyrazinyl, isothiazolopyrazinyl, pyrrolopyridazinyl, furopyridazinyl, thienopyridazinyl, imidazolopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, pyrazolopyridazinyl, isoxazolopyridazinyl or isothiazolopyridazinyl; Het^1 is independently optionally substituted with up to a total of four substituents independently selected from R^8, R^9, R^{10} and R^{11}; wherein R^8, R^9, R^{10} and R^{11} are each taken separately and are each independently halo, formyl, $(C_1$-$C_6)$alkoxycarbonyl, $(C_1$-$C_6)$alkylenyloxycarbonyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $C(OH)R^{12}R^{13}$, $(C_1$-$C_4)$alkylcarbonylamido, $(C_3$-$C_7)$cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, $(C_1$-$C_4)$alkylsulfenyl, $(C_1$-$C_4)$alkylsulfonyl, $(C_3$-$C_7)$cycloalkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to three fluoro or $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkoxy-$(C_1$-$C_4)$alkyl, $(C_1$-$C_4)$alkyl optionally substituted with up to five fluoro and $(C_1$-$C_4)$alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in

the definition of R^8, R^9, R^{10} and R^{11} are optionally substituted with up to two substituents independently selected from hydroxy, halo, C_1-C_4)alkyl, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, C_1-C_4)alkyl-phenyl optionally substituted in the phenyl portion with one Cl, Br, OMe, Me or SO_2-phenyl wherein said SO_2-phenyl is optionally substituted in the phenyl portion with one Cl, Br, OMe, Me, (C_1-C_4)alkyl optionally substituted with up to five fluoro, or (C_1-C_4)alkoxy optionally substituted with up to three fluoro;

R^{12} and R^{13} are each independently hydrogen or (C_1-C_4)alkyl;

Het^2 and Het^3 are each independently imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy; Het^2 and Het^3 are each independently optionally substituted with up to a total of four substituents independently selected from R^{14}, R^{15}, R^{16} and R^{17}, wherein R^{14}, R^{15}, R^{16} and R^{17} are each taken separately and are each independently halo, formyl, (C_1-C_6)alkoxycarbonyl, (C_1-C_6)alkylenyloxycarbonyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, $C(OH)R^{18}R^{19}$, (C_1-C_4)alkylcarbonylamido, (C_3-C_7)cycloalkylcarbonylamido, phenylcarbonylamido, phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, (C_1-C_4)alkylsulfenyl, (C_1-C_4)alkylsulfonyl, (C_3-C_7)cycloalkyl, (C_1-C_4)alkyl optionally substituted with up to three fluoro or (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said phenyl, naphthyl, imidazolyl, pyridyl, triazolyl, benzimidazolyl, oxazolyl, isoxazolyl, thiazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, thienyl, benzothiazolyl, pyrrolyl, pyrazolyl, quinolyl, isoquinolyl, benzoxazolyl, pyridazinyl, pyridyloxy, pyridylsulfonyl, furanyl, phenoxy, thiophenoxy, in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to three substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to five fluoro; said imidazolyl, oxazolyl, isoxazolyl, thiazolyl and pyrazolyl in the definition of R^{14}, R^{15}, R^{16} and R^{17} are optionally substituted with up to two

substituents independently selected from hydroxy, halo, hydroxy-(C_1-C_4)alkyl, (C_1-C_4)alkoxy-(C_1-C_4)alkyl, (C_1-C_4)alkyl optionally substituted with up to five fluoro and (C_1-C_4)alkoxy optionally substituted with up to three fluoro; and

R^{18} and R^{19} are each independently hydrogen or (C_1-C_4)alkyl;

X and Y together are CH_2-CH(OH)-Ar or CH_2-C(O)-Ar, or

X is a covalent bond, NR^{20} or CHR^{21}, wherein, R^{20} is (C_1-C_3)alkyl or a phenyl that is optionally substituted with one or more substituents selected from OH, F, Cl, Br, I, CN, CF_3, (C_1-C_6)alkyl, O-(C_1-C_6)alkyl, $S(O)_n$-(C_1-C_6)alkyl and SO_2—$NR^{22}R^{23}$, and R^{21} is hydrogen or methyl, and

Y is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from Ar, OH, F, Cl, Br, I, CN, CF_3, (C_1-C_6)alkyl, O-(C_1-C_6)alkyl, $S(O)_n$-(C_1-C_6)alkyl and SO_2—$NR^{22}R^{23}$;

Ar is a phenyl or naphthyl ring optionally substituted with one or more substituents selected from F, Cl, Br, I, CN, CF_3, (C_1-C_6)alkyl, O-(C_1-C_6)alkyl, $S(O)_n$-(C_1-C_6)alkyl and SO_2—$NR^{22}R^{23}$;

n is independently for each occurrence 0, 1 or 2;

R^{22} is independently for each occurrence H, (C_1-C_6)alkyl, phenyl or naphthyl; and

R^{23} is independently for each occurrence (C_1-C_6)alkyl, phenyl or naphthyl,

provided that when R^3 is NR^6R^7, then A is SO_2,

and a second compound that is a cyclooxygenase-2 inhibitor, a prodrug of said second compound or a pharmaceutically acceptable salt of said second compound or said prodrug.

21. A therapeutic method of claim 20 wherein said first compound is a compound of formula I, wherein A is SO_2; R^1 and R^2 are each hydrogen; R^3 is Het^1, wherein Het^1 is 5H-furo-[3,2c]pyridin-4-one-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl, indol-2-yl, indol-3-yl, benzofuran-2-yl, benzothien-2-yl, imidazo[1,2a]pyridin-3-yl, pyrrol-1-yl, imidazol-1-yl, indazol-1-yl, tetrahydroquinol-1-yl or tetrahydroindol-1-yl, wherein said Het^1 is optionally independently substituted with up to a total of two substituents each independently selected from fluoro, chloro, bromo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, trifluoromethyl, hydroxy, benzyl or phenyl; said benzyl and phenyl are each optionally independently substituted with up to three halo, (C_1-C_6)alkyl, (C_1-

C_6)alkoxy, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylsulfinyl, (C_1-C_6)alkylsulfenyl, trifluoromethyl or hydroxy, or a prodrug thereof or a pharmaceutically acceptable salt of said compound or prodrug.

22. A therapeutic method of claim 21 wherein Het^1 is indol-2-yl, benzofuran-2-yl, benzothiophen-2-yl, furano[2,3b]pyridin-2-yl, thieno[2,3b]pyridin-2-yl or imidazo[1,2a]pyridin-4-yl, wherein said Het^1 is optionally independently substituted with up to a total of two substituents independently selected from fluoro, chloro, bromo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, trifluoromethyl and phenyl; said phenyl being optionally substituted with up to two substituents independently selected from fluoro, chloro and (C_1-C_6)alkyl.

23. A therapeutic method of claim 20 wherein said first compound is selected from: 6-(3-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-bromo-2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-trifluoromethyl-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-bromo-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-methoxy-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3-bromo-benzenesulfonyl)-2H-pyridazin-3-one;

6-(biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(4'-fluoro-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(4'-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(3',5'-bis-trifluoromethyl-biphenyl-4-sulfonyl)-2H-pyridazin-3-one;

6-(biphenyl-2-sulfonyl)-2H-pyridazin-3-one;

6-(4'-trifluoromethyl-biphenyl-2-sulfonyl)-2H-pyridazin-3-one;

6-(2-hydroxy-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(3-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,3-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,5-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(4-chloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,3-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,4-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,4-difluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2,6-dichloro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-chloro-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one;

6-(2-bromo-4-fluoro-benzenesulfonyl)-2H-pyridazin-3-one; and

6-(naphthalene-1-sulfonyl)-2H-pyridazin-3-one,

or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

24. A therapeutic method of claim 20 wherein said second compound is selected from celecoxib, rofecoxib and etoricoxib or a prodrug thereof or a pharmaceutically acceptable salt of said compound or said prodrug.

25. A therapeutic method of claim 20 wherein said first compound is administered in an aldose reductase inhibiting amount.

26. A therapeutic method of claim 20 wherein said second compound is administered in a cyclooxygenase-2 inhibiting amount.

27. A therapeutic method of claim 25 wherein said second compound is administered in a cyclooxygenase-2 inhibiting amount.

28. A therapeutic method of claim 20 wherein said mammal is a human.